PREGNANCY, HEART DISEASE & STROKE IN WOMEN

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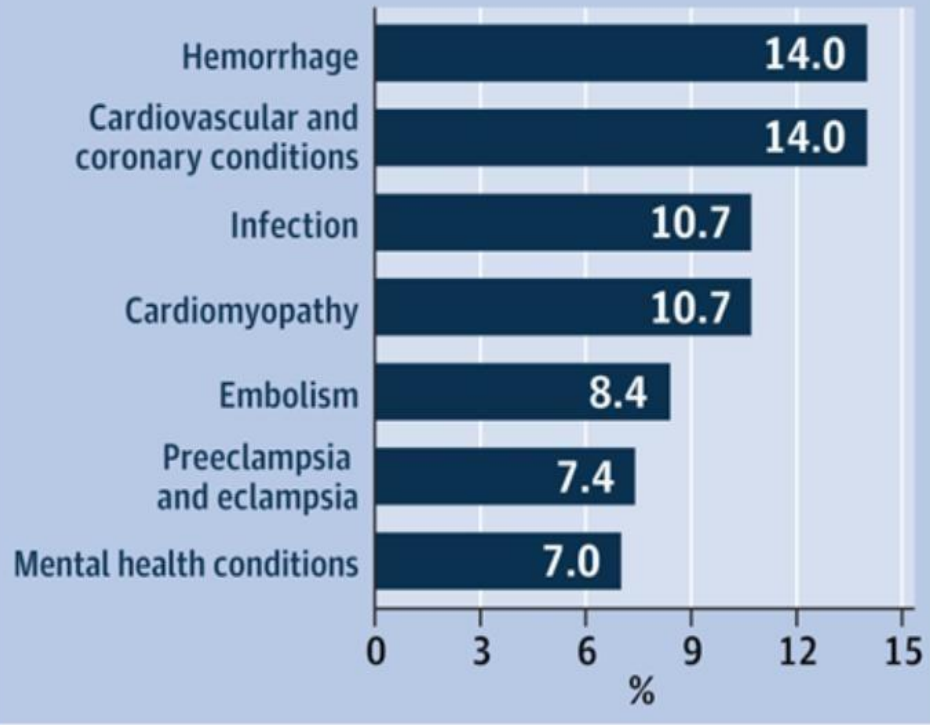
Pregnancy-Related Deaths in the US

Leading underlying causes of pregnancy-related deaths



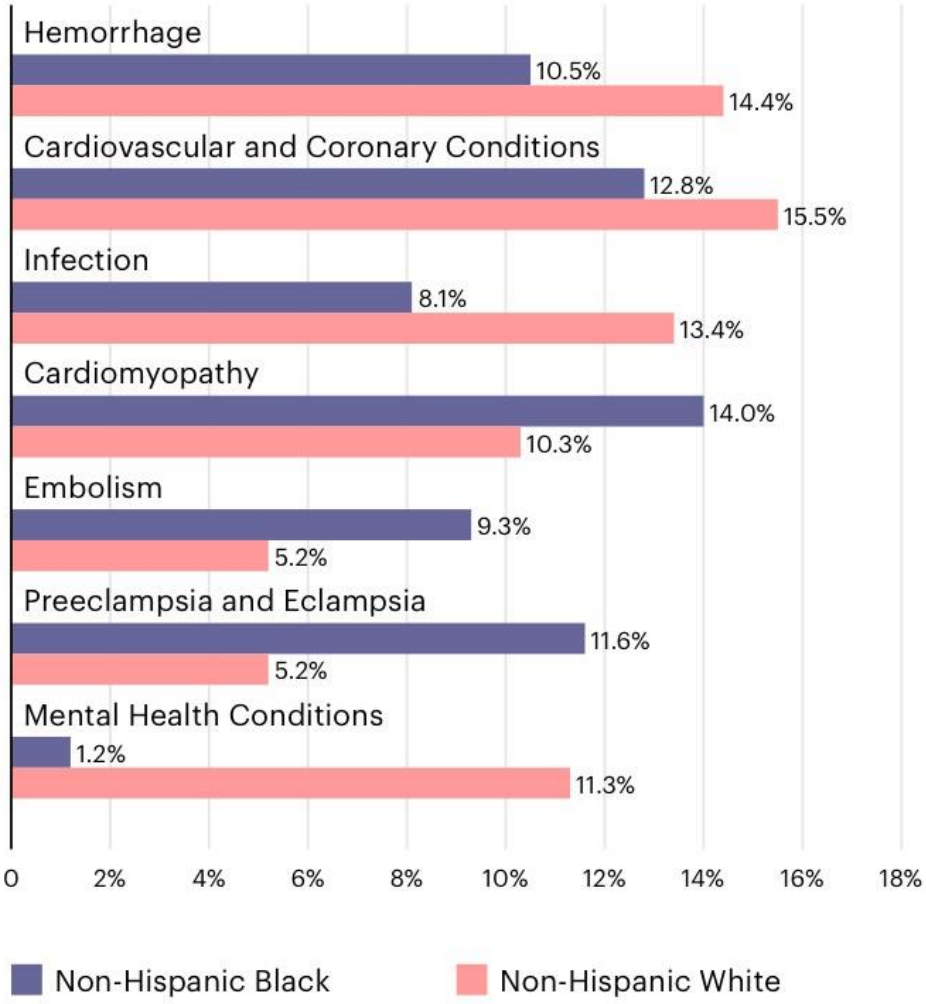
Preventability among pregnancy-related deaths

70.0%
of pregnancy-related deaths from hemorrhage are preventable

68.2%
of pregnancy-related deaths from cardiovascular and coronary conditions are preventable

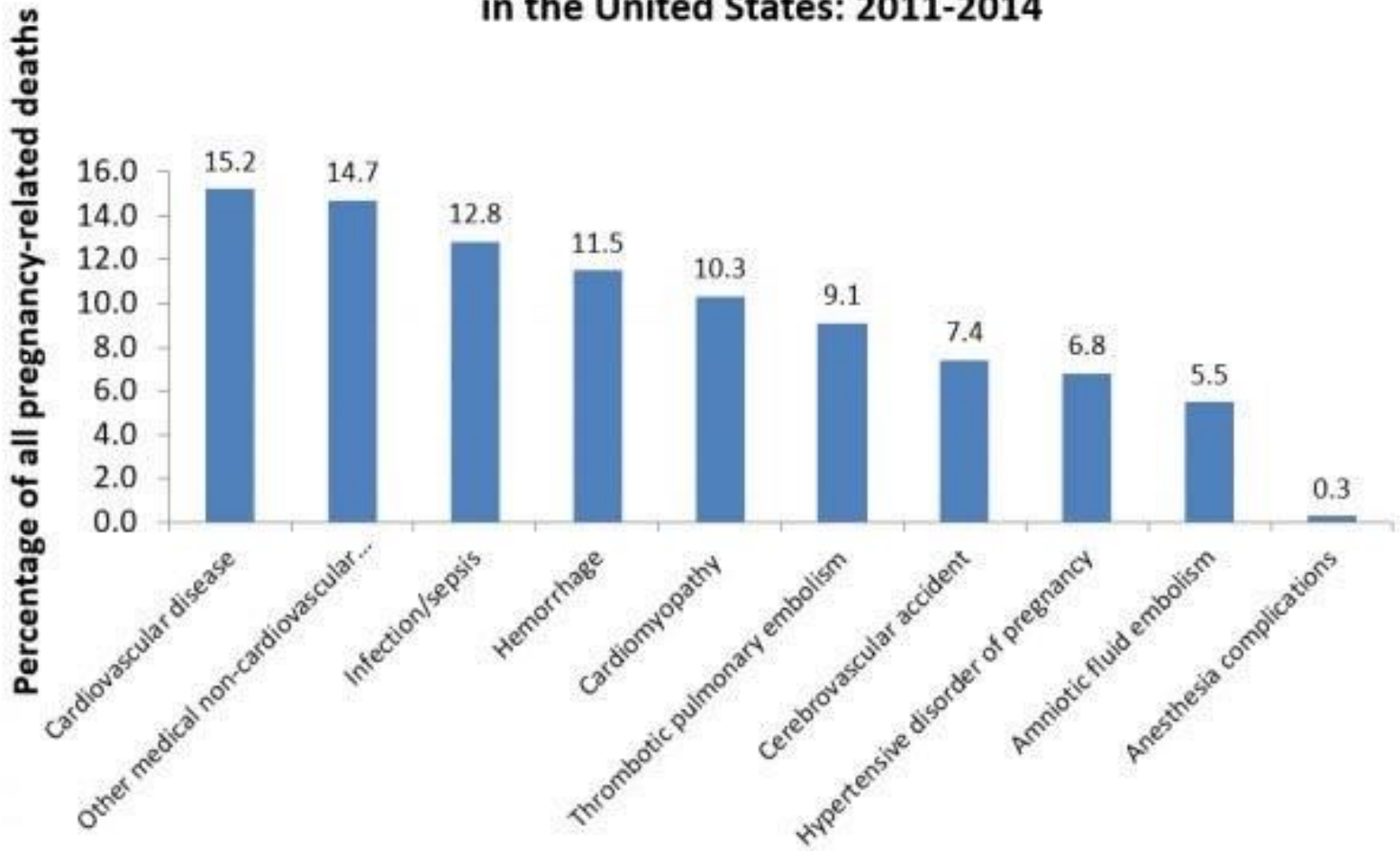
Source: Review to Action. *Report From Nine Maternal Mortality Review Committees.* https://reviewtoaction.org. Published 2018.

Leading Underlying Causes of Pregnancy-Related Deaths, by Race-Ethnicity



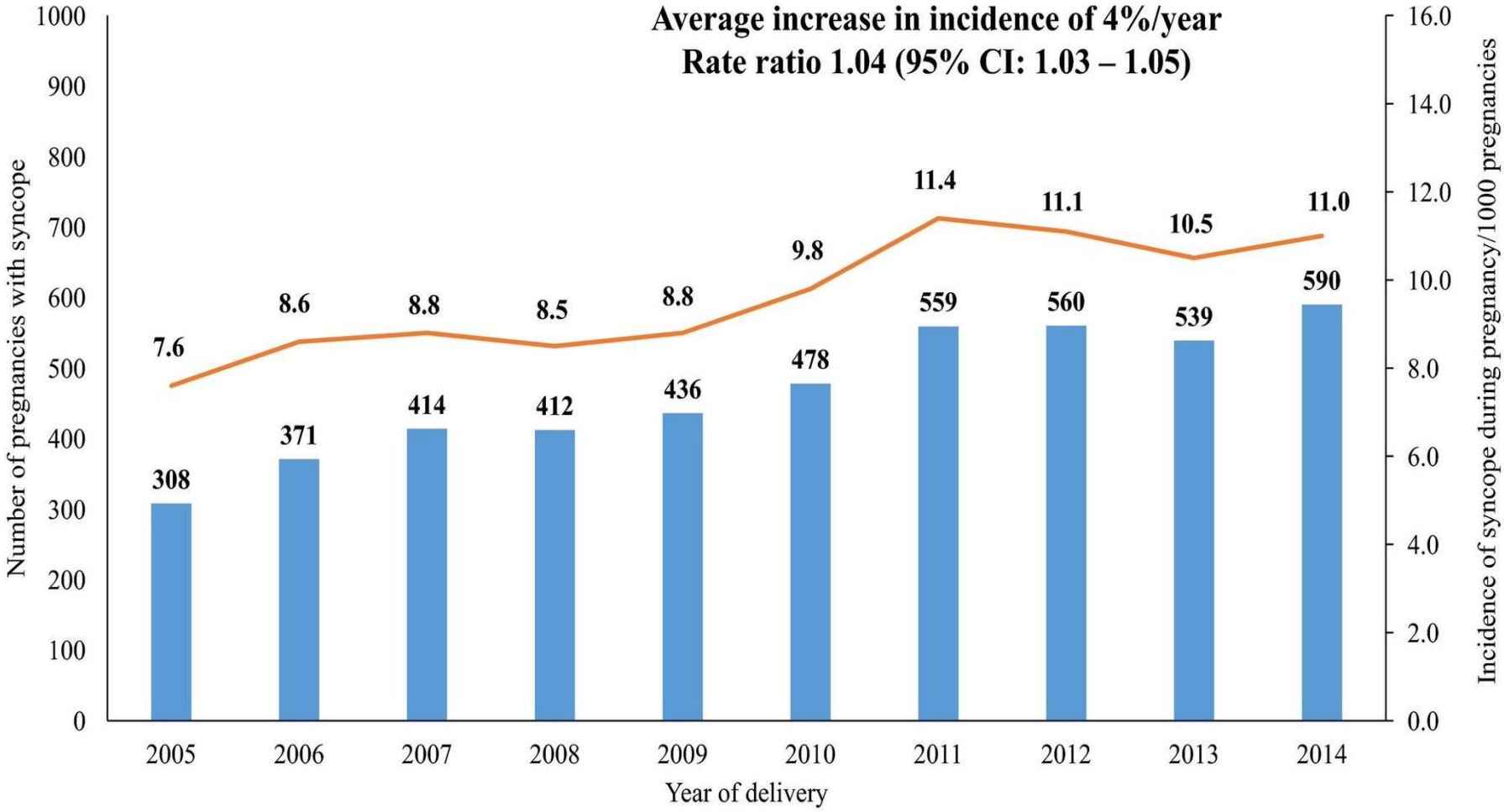
Source: CDC Foundation 2018

Causes of pregnancy-related death in the United States: 2011-2014



Note: The cause of death is unknown for 6.5% of all pregnancy-related deaths.

SYNCOPE DURING PREGNANCY



PREGNANCY COMPLICATIONS AND HEART DISEASE

Women who experience certain pregnancy and delivery complications are at a greater risk of heart disease and stroke later in life.

COMPLICATIONS THAT CAN INCREASE RISK:

- High blood pressure (HBP)
- Pre-eclampsia (HBP with certain other signs or symptoms)
- Baby is pre-term (born before 37 weeks)
- Baby is small for gestational age (weighs much less than normal, given timing of delivery)
- Gestational diabetes (high blood sugar in pregnancy)

5 STEPS TO A HEART HEALTHY PREGNANCY:

1. Get early and regular prenatal care.

2. Exercise regularly and keep weight gain within general guidelines.

3. Do not smoke (ever!) or drink alcohol during pregnancy.

4. Eat regular, healthful meals and take prenatal vitamins with folate during pregnancy.

5. Limit salt and caffeine, which can increase blood pressure or cause an irregular heartbeat in the mother.

Talk to your health care provider about heart disease and stroke and #getHeartChecked.

AWHONN PROMOTING THE HEALTH OF WOMEN AND NEWBORNS | WOMEN'S HEART ALLIANCE | ACOG

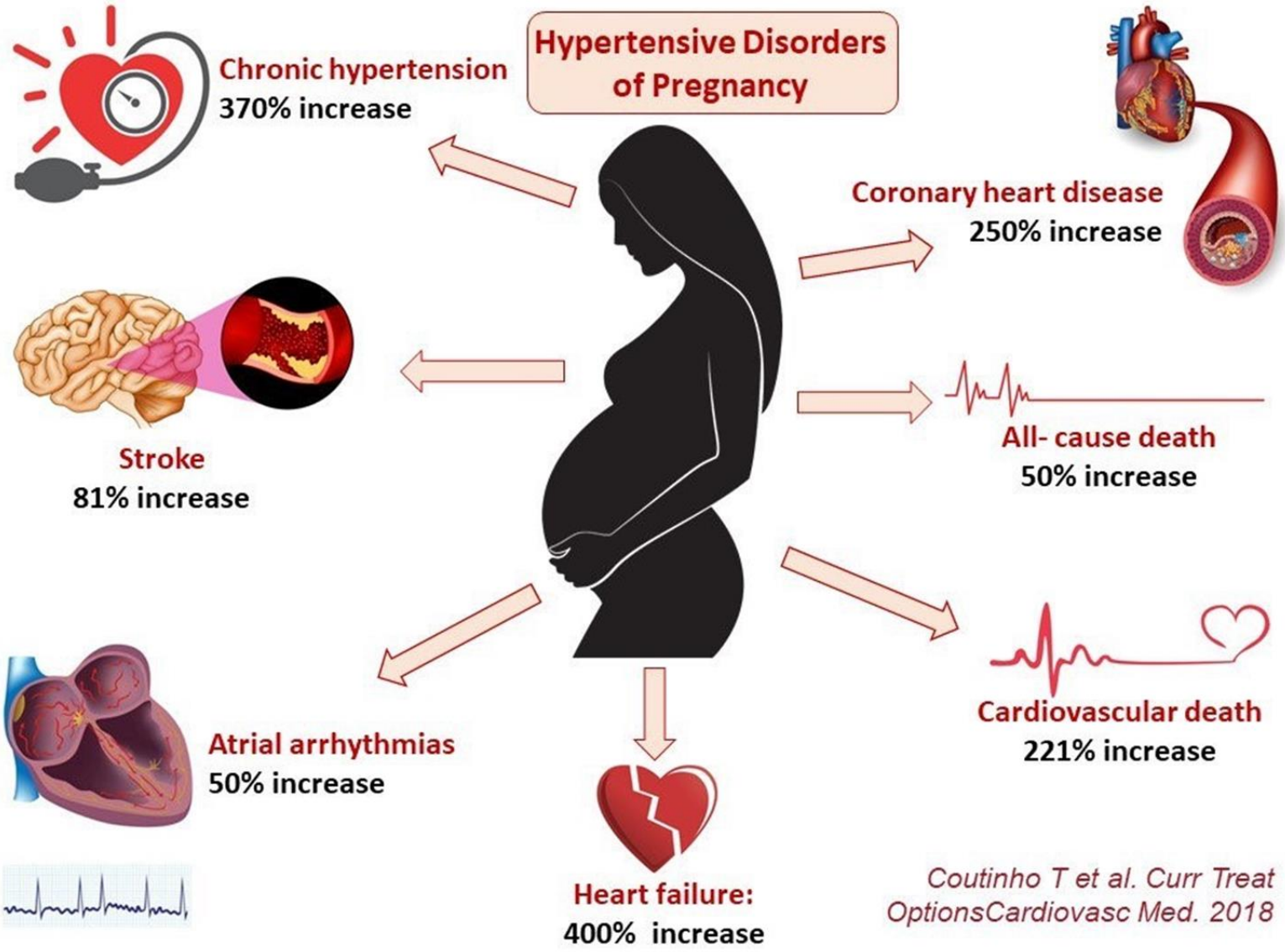
emoryhealthcare.org/womensheart

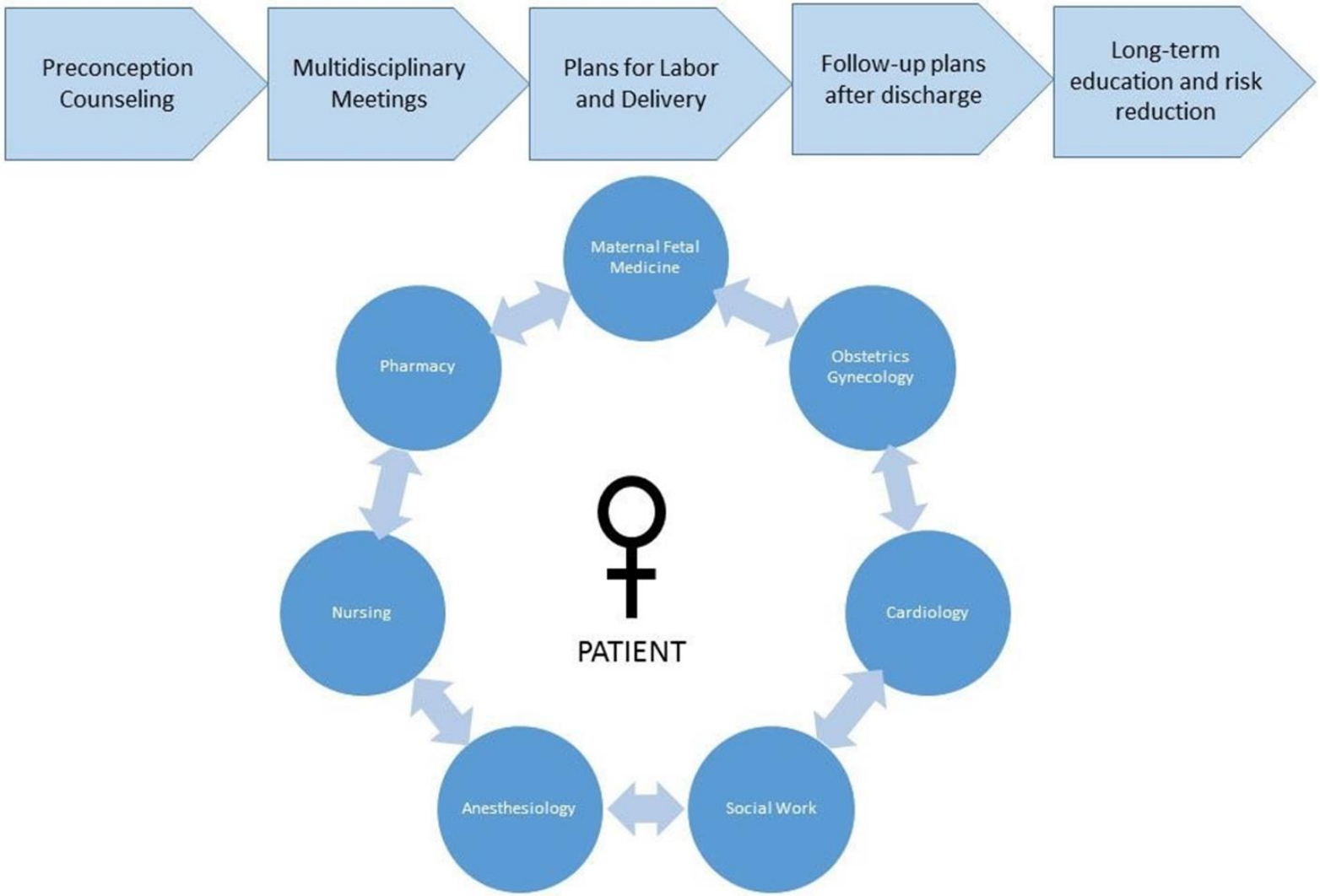
EMORY WOMEN'S HEART CENTER

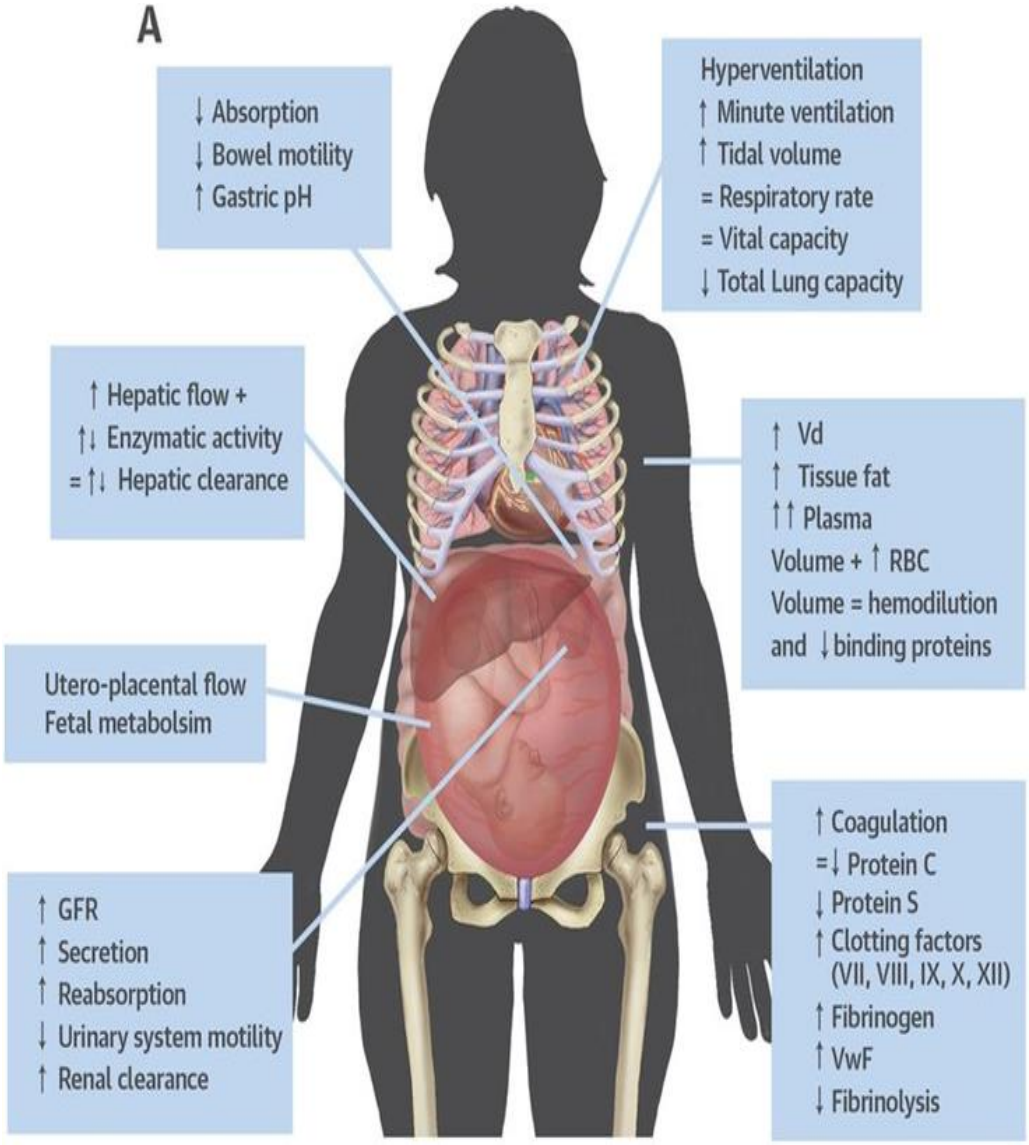
PREGNANCY IS FIRST STRESS TEST

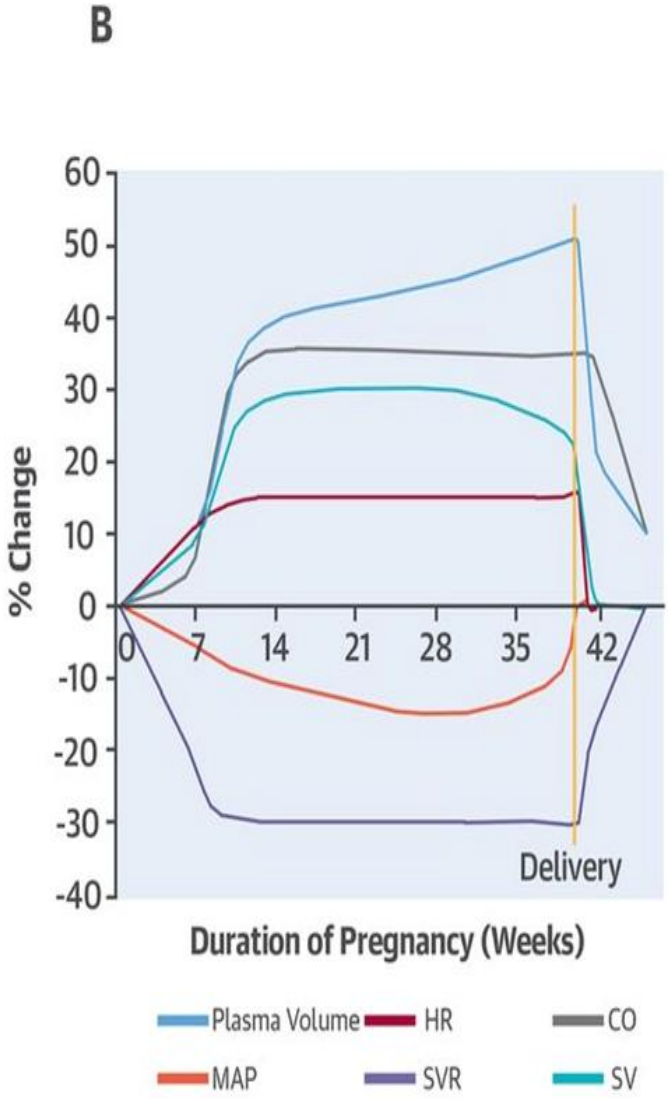
PREGNANCY COMPLICATIONS

- Detailed pregnancy history integral component of risk assessment for women
- Pregnancy complications: preeclampsia, gestational diabetes, pregnancy-induced hypertension, preterm delivery are early indicators ↑ CV risk
- Cardiovascular, metabolic stress of pregnancy → potential for early prediction future CV risk
- Preeclampsia, gestational hypertension →↑ CVD risk
  - 3-6X ↑ subsequent hypertension
  - 2x ↑ ischemic heart disease, stroke
  - Residual endothelial dysfunction, association with ↑ CAC
- Gestational diabetes → 7x ↑ risk type 2 DM


Hypertensive Disorders of Pregnancy
Chronic hypertension
370% increase
Coronary heart disease
250% increase
Stroke
81% increase
All- cause death
50% increase
Atrial arrhythmias
50% increase
Cardiovascular death
221% increase
Heart failure:
400% increase
Coutinho T et al. Curr Treat OptionsCardiovasc Med. 2018


Preconception Counseling
Multidisciplinary Meetings
Plans for Labor and Delivery
Follow-up plans after discharge
Long-term education and risk reduction
Maternal Fetal Medicine
Obstetrics Gynecology
Cardiology
Social Work
Anesthesiology
Nursing
Pharmacy
PATIENT


A
↓ Absorption
↓ Bowel motility
↑ Gastric pH
Hyperventilation
↑ Minute ventilation
↑ Tidal volume
= Respiratory rate
= Vital capacity
↓ Total Lung capacity
↑ Hepatic flow +
↑↓ Enzymatic activity
= ↑↓ Hepatic clearance
↑ Vd
↑ Tissue fat
↑↑ Plasma
Volume + ↑ RBC
Volume = hemodilution
and ↓ binding proteins
Utero-placental flow
Fetal metabolsim
↑ GFR
↑ Secretion
↑ Reabsorption
↓ Urinary system motility
↑ Renal clearance
↑ Coagulation
=↓ Protein C
↓ Protein S
↑ Clotting factors
(VII, VIII, IX, X, XII)
↑ Fibrinogen
↑ VwF
↓ Fibrinolysis


B
% Change
60
50
40
30
20
10
0
-10
-20
-30
-40
0
7
14
21
28
35
42
Delivery
Duration of Pregnancy (Weeks)
Plasma Volume
HR
CO
MAP
SVR
SV

RISK FACTORS FOR PREGNANCY-INDUCED HTN

- Obesity
- Chronic HTN
- Gestational HTN
- First time pregnancy
- Multiple pregnancy
- Pre-existing vascular disease
- Personal or family hx of preeclampsia
- Collagen (connective tissue) vascular disease
- Age >40 years
- Diabetes
- Renal disease

Bushnell 2014 Circ and JACC

Table 2. How to Differentiate Common Signs and Symptoms of Normal Pregnancy Versus Those That Are Abnormal and Indicative of Underlying Cardiac Disease

	ROUTINE CARE	CAUTION*†	STOP†‡
	Reassurance	Nonemergent Evaluation	Prompt Evaluation Pregnancy Heart Team
History of CVD	None	None	Yes
Self-reported symptoms	None or mild	Yes	Yes
Shortness of breath	No interference with activities of daily living; with heavy exertion only	With moderate exertion, new-onset asthma, persistent cough, or moderate or severe OSA§	At rest; paroxysmal nocturnal dyspnea or orthopnea; bilateral chest infiltrates on CXR or refractory pneumonia
Chest pain	Reflux related that resolves with treatment	Atypical	At rest or with minimal exertion
Palpitations	Few seconds, self-limited	Brief, self-limited episodes; no lightheadedness or syncope	Associated with near syncope
Syncope	Dizziness only with prolonged standing or dehydration	Vasovagal	Exertional or unprovoked
Fatigue	Mild	Mild or moderate	Extreme
Vital signs	Normal		
HR (beats per minute)	<90	90–119	≥120
Systolic BP (mm Hg)	120–139	140–159	≥160 (or symptomatic low BP)
RR (per minute)	12–15	16–25	≥25
Oxygen saturation	>97%	95–97%	<95% (unless chronic)
Physical examination	Normal		
JVP	Not visible	Not visible	Visible >2 cm above clavicle
Heart	S3, barely audible soft systolic murmur	S3, systolic murmur	Loud systolic murmur, diastolic murmur, S4
Lungs	Clear	Clear	Wheezing, crackles, effusion
Edema	Mild	Moderate	Marked

Abbreviations: BP, blood pressure; CVD, cardiovascular disease; CXR, chest x-ray; HR, heart rate; JVP, jugular venous pressure; OSA, obstructive sleep apnea; RR, respiratory rate.

*If unclear, any combination of factors in the yellow column that add up to 4 or more should prompt further evaluation.

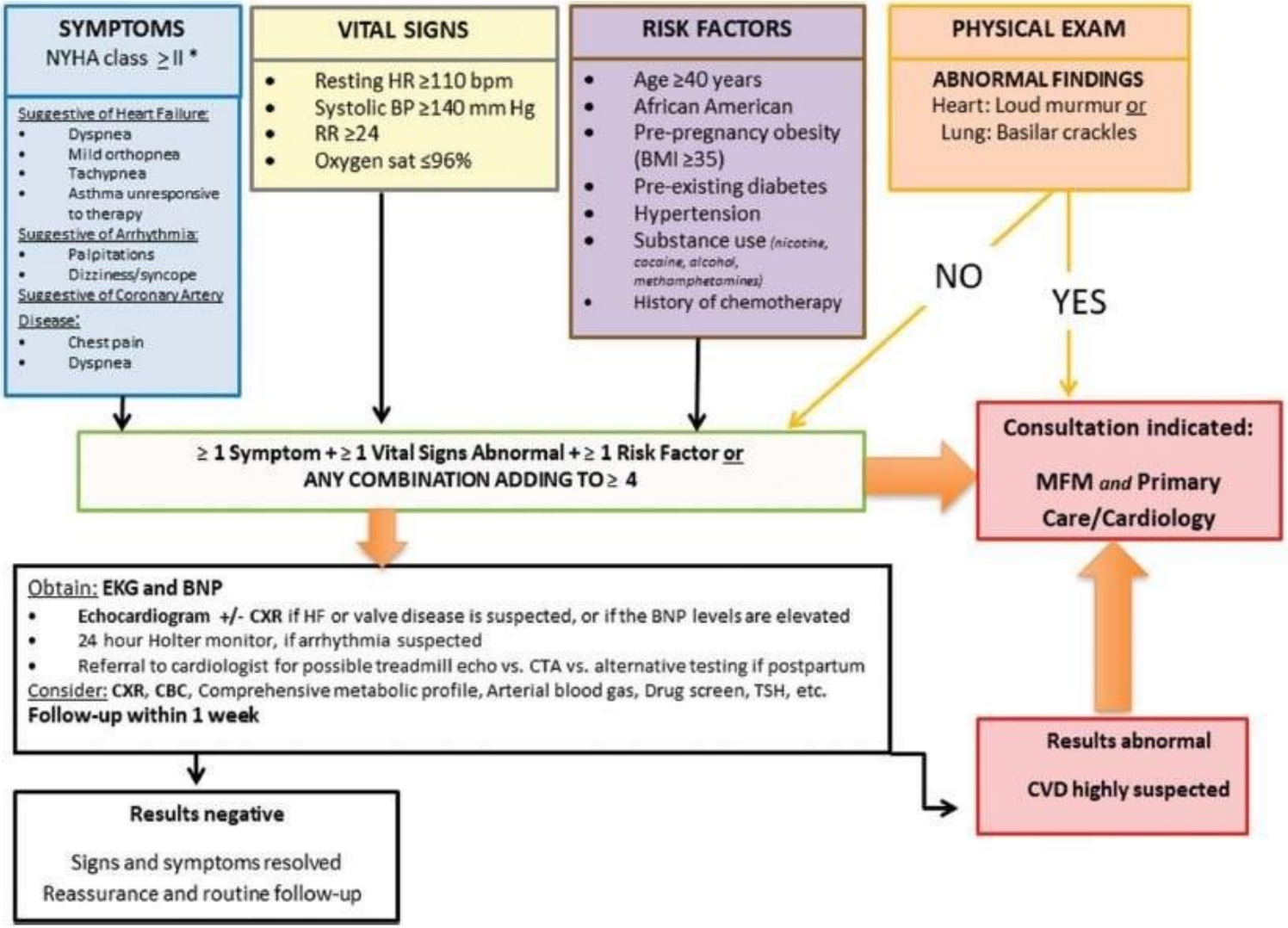


Figure 1. Cardiovascular Disease Assessment in Pregnant and Postpartum Women. *The NYHA Functional Classification is available at http://www.heart.org/HEARTORG/Conditions/HeartFailure/AboutHeartFailure/Classes-of-Heart-Failure_UCM_306328_Article.jsp. Abbreviations: BMI, body mass index; BNP, brain natriuretic peptide; BP, blood pressure; CBC, complete blood count; CVD, cardiovascular disease; CXR, chest x-ray; EKG, electrocardiogram; HR, heart rate; MFM, maternal–fetal medicine; TSH, thyroid stimulating hormone; NYHA, New York Heart Association; RR, respiratory rate. (Modified from California Department of Public Health, 2017; supported by Title V funds. Developed in partnership with California Maternal Quality Care Collaborative Cardiovascular Disease in Pregnancy and Postpartum Taskforce. Visit www.CMQCC.org for details.)

Table 1. Pregnancy-Related Complications

Condition and Background	Postpartum Test and Screening	Management Considerations	Long-Term Goals
Gestational Diabetes			
Women with gestational diabetes have a sevenfold increased risk of developing type 2 diabetes.	Fasting plasma glucose or 75-g, 2-hour OGTT at 4–12 weeks postpartum; screening should happen every 3 years. If the initial test in the postpartum shows prediabetes, they should be screened for diabetes yearly.	Encourage breastfeeding Women with impaired fasting glucose, impaired glucose tolerance, or diabetes should be referred for preventive or medical therapy.	Early detection of overt diabetes; diabetes prevention
Diabetes			
Poorly controlled diabetes increases risk of nephropathy, neuropathy, retinopathy, cardiovascular disease, and other chronic morbidity. Poorly controlled diabetes is associated with birth defects in the next pregnancy.	Patients should demonstrate good control of blood sugars with hemoglobin A_{1c} <6.5	Weight management Referral for preventive and medical therapy For women with type 1 diabetes, thyroid screening once if never completed. In subsequent pregnancies, consider low-dose aspirin 81 mg QD to reduce pre-eclampsia risk	Goal Hemoglobin A_{1c}: 6.0–6.5% (42–48 mmol/L) recommended Achieve without hypoglycemia
Preeclampsia and Gestational Hypertension			
Women with preeclampsia have an increased risk of recurrence in subsequent pregnancies. These women also have a two-fold increased risk of subsequent cardiovascular disease.	Blood pressure monitoring for 72 hours postpartum Blood pressure monitoring 7–10 days after delivery Postpartum blood pressure check	In subsequent pregnancies, consider low-dose aspirin 81 mg QD to reduce preeclampsia risk	Maintain blood pressure <120/80 Maintain healthy weight
Chronic Hypertension			
Uncontrolled hypertension in the postpartum period	Blood pressure monitoring for 72 hours postpartum	In subsequent pregnancies, consider low-dose aspirin	Maintain blood pressure <120/80

HTN- CLASS I RECOMMENDATIONS

- Women with chronic primary or secondary hypertension, or previous pregnancy-related hypertension, should take **low dose aspirin** from the 12th week of gestation until delivery
- **Calcium** supplementation (of at least 1g/d, orally) should be considered for women with low dietary intake of calcium (<600 mg/d) to prevent preeclampsia

HTN- CLASS I RECOMMENDATIONS

Severe hypertension in pregnancy should be treated with safe & effective antihypertensive medications such as **methyldopa, labetalol and nifedipine**, with consideration of maternal & fetal side effects

RECOMMENDATIONS: TREATMENT OF HTN POSTPARTUM

Due to the increased risk of future HTN & stroke 1-30 years after delivery in women with a history of preeclampsia it is reasonable to:

(1) evaluate all women **starting 6 mo to 1 year** postpartum & all those with a HX of preeclampsia/eclampsia

(2) document their history is a CVD risk factor

(3) Evaluate& treat for **CVD risk factors** including hypertension, obesity, smoking & dyslipidemia

STROKE & PREGNANCY

- Pregnancy-related HTN is the leading cause of both hemorrhagic & ischemic stroke in pregnant & post partum women
- Stroke is not common during pregnancy
- Risk for stroke is higher in

  pregnant women (34 per 100K) vs nonpregnant women (21 per 100K)
- Highest risk in the 3rd trimester & post partum

PREGNANCY SCAD & NON-PREG SCAD

	P-SCAD -54	NP-SCAD -269
Presentation	STEMI- 57% EF<35%- 26%	STEMI- 36% EF<35%- 10%
Assoc with FMD	42%	64%
Pregnancy Hx	Multiparous- 91% Infertility tx- 28% Pre-eclampsia- 11%	76% 16% 6%
LM SCAD	24%	5%
Multivessel SCAD	33%	14%
Age Race	35 yrs 89% Caucasian	47 yrs 97 Caucasian

Tweet, JACC July 2017

CENTRAL ILLUSTRATION: Features of Pregnancy-Associated Spontaneous Coronary Artery Dissection

Spontaneous Coronary Artery Dissection (SCAD)

A coronary artery hematoma ± tear limits coronary blood flow to the myocardium

Hematoma

Tear in arterial wall

Pregnancy-associated SCAD (P-SCAD)

- **Frequently occurs in first month postpartum** (majority of these within first week after delivery)
- **P-SCAD presentation often severe:**
  - ST-segment elevation myocardial infarction
  - Reduced left ventricular function
  - Left main and/or multivessel SCAD
- **Compared to non-pregnancy-associated SCAD:**
  - P-SCAD has a higher risk presentation
  - P-SCAD patients are older at time of first childbirth and more frequently have history of multiple pregnancies
  - P-SCAD patients have fewer extracoronary vascular abnormalities

Recommended areas of P-SCAD research:

- Hemodynamic stressors
- Hormonal fluctuations
- Oxytocin release in breastfeeding mothers
- Older, multiparous mothers
- Relationship to:
  - Eclampsia/ pre-eclampsia
  - Peripartum cardiomyopathy
  - Fibromuscular dysplasia and other extracoronary vascular abnormalities

Tweet, M.S. et al. J Am Coll Cardiol. 2017;70(4):426–35.

PREVENTION OF HEART DISEASE IN WOMEN

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WOMEN'S HEART
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Statistics for CVD in America

- 840,678 Americans died of cardiovascular disease (CVD= Heart & Stroke) in 2016
- Every 40 seconds, someone has a heart attack AND someone has a stroke
- Nearly half of all Americans adults have some form of CVD (Coronary disease, High blood pressure and Stroke)
- AHA Heart Disease and Stroke Stats- 2019 Update/ Circulation

AHA STATISTICAL UPDATE 2019

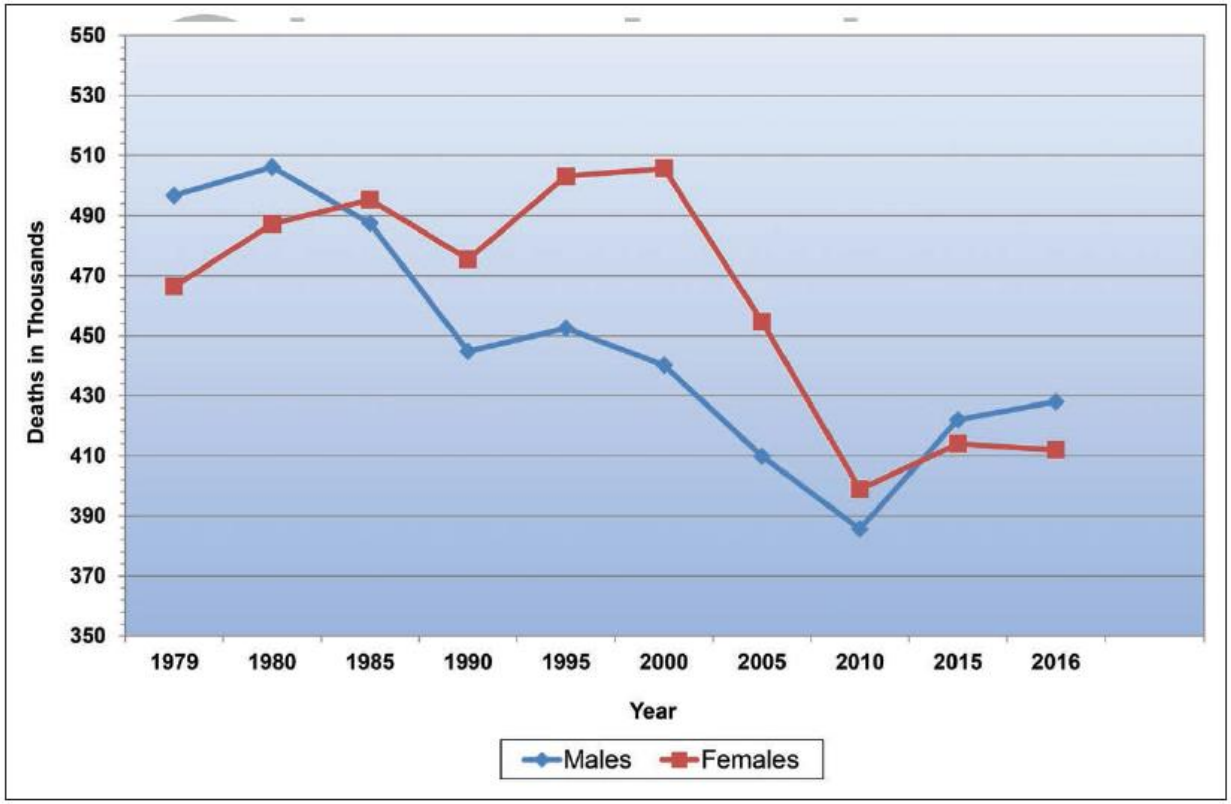
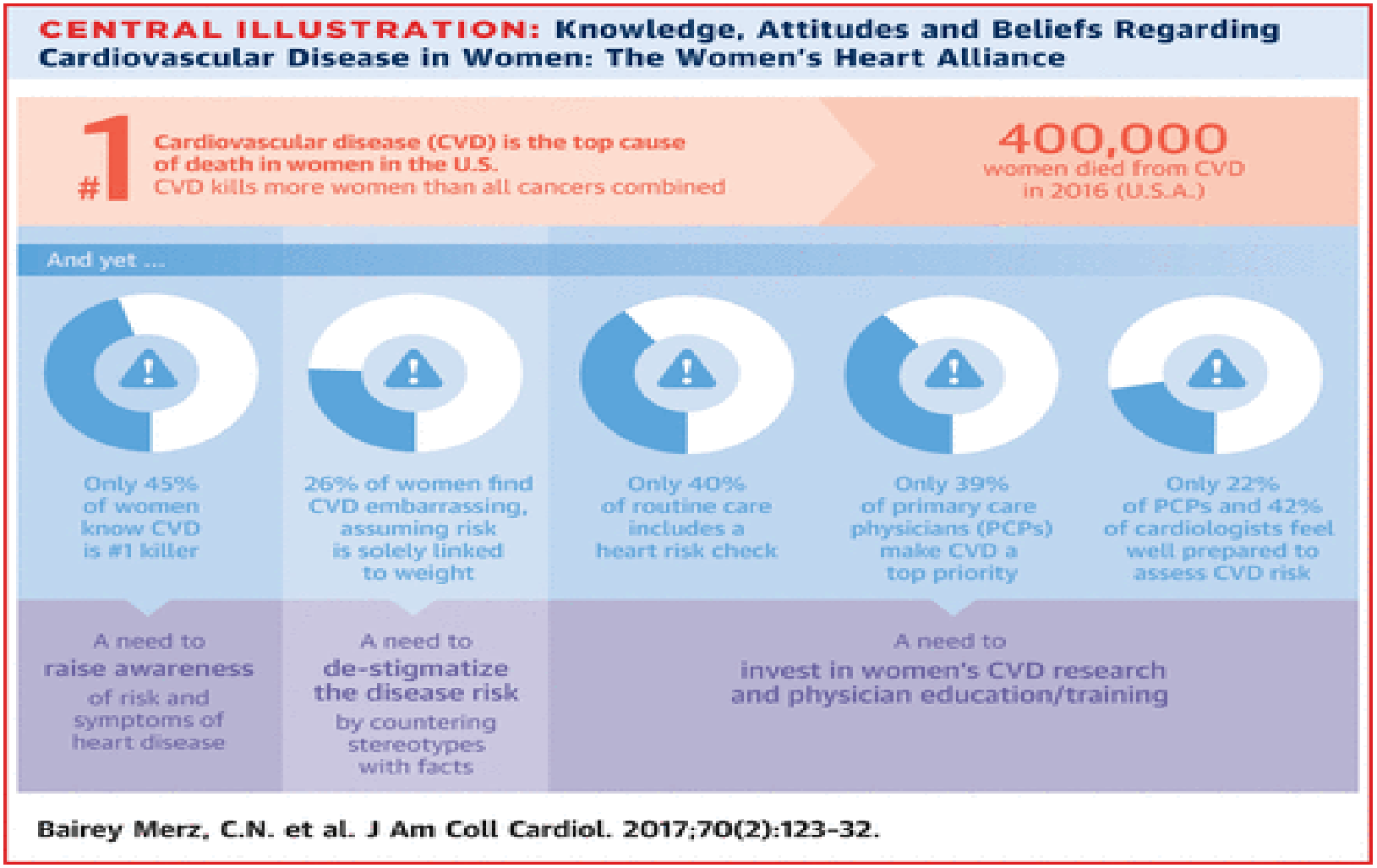


Chart 13-16. Cardiovascular disease (CVD) mortality trends for males and females (United States, 1979–2016).
CVD excludes congenital cardiovascular defects (*International Classification of Diseases, 10th Revision* [*ICD-10*] codes I00–I99). The overall comparability for cardiovascular disease between the *International Classification of Diseases, 9th Revision* (1979–1998) and *ICD-10* (1999–2015) is 0.9962. No comparability ratios were applied.
Source: National Center for Health Statistics and National Heart, Lung, and Blood Institute.

EJ Benjamin, *Circulation* March 2019

PATIENT AWARENESS, STIGMA, AND PHYSICIAN AWARENESS AND TRAINING EFFECT CVD CARE IN WOMEN



Bairey Merz, C.N. et al. J Am Coll Cardiol. 2017;70(2):123–32.

Emerging Risk Factors

SLE: 3-fold higher risk of IHD events [18]
Rheumatoid arthritis: elevates IHD risk as much as DM [18]

Gestational diabetes
- 4-fold higher risk of DM
- 59% higher risk of MI[17]

Hypertension in pregnancy:
- Gestational HTN and preclampsia: 3-fold higher risk of IHD[18]

Early menopause confers 4.5 times higher risk of IHD[99]

Depression is more prevalent in women
Doubles the risk of IHD[16]

Traditional Risk Factors

Menopause results in ↑ TG, ↑ LDL, ↓ HDL
Women are less likely to achieve lipid goals (OR 0.50) [97]

80% of women ≥75 have HTN
Only 29% have adequate BP control [22,98]

Diabetes confers a 45% higher risk of IHD[16]

Smoking confers a 25% higher risk of IHD[96]

Obesity confers a higher risk of IHD in women (64% vs 46%)[94]

Women have a higher prevalence of inactivity
25% of US women get no regular physical activity[95]

Family History of premature atherosclerosis confers a 2 fold higher risk of IHD in men and women[100]

SEX-BASED DISPARITIES IN OUTCOMES & QUALITY OF CARE

- Less diagnostic testing or angiography
- Delay in Reperfusion
- Fewer Revascularizations
- Less Pharmacotherapy
- Less Cardiac Rehab referral & completion
- Higher morbidity after MI
- Higher in-hospital mortality with angina, STEMI & ACS
- Higher mortality in younger women (<55yrs)

CVD IN WOMEN

- Women have a higher prevalence of angina
- Women have a lower burden of obstructive CAD
- Women have a poorer prognosis compared to men
- Clinical presentation- chest pain most common but also weakness, dyspnea, nausea, and neck, jaw and back pain

- WISE investigators, NHLBI WISE study, Am Heart Journal 2001;141:735-741

RECOMMENDATIONS FOR PREVENTION OF HEART DISEASE

- Evaluation after pregnancy complication- Gest DM, HTN, Preeclampsia, Eclampsia
- Evaluation of CVD risks in Rheumatic/ Autoimmune disorders
- Close observation after Breast Cancer, Chemotherapy, Radiation
- Close observation with Depression/Stress, domestic violence, trauma, etc

RECOMMENDATIONS FOR PREVENTION OF HEART DISEASE IN ALL WOMEN

- HTN control
- DM control
- Lipid control
- Smoking Cessation
- Obesity- BMI<25 ideal
- Lifestyle- Diet and Physical activity

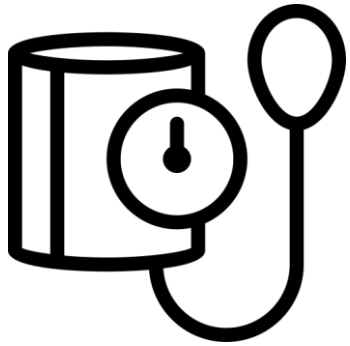
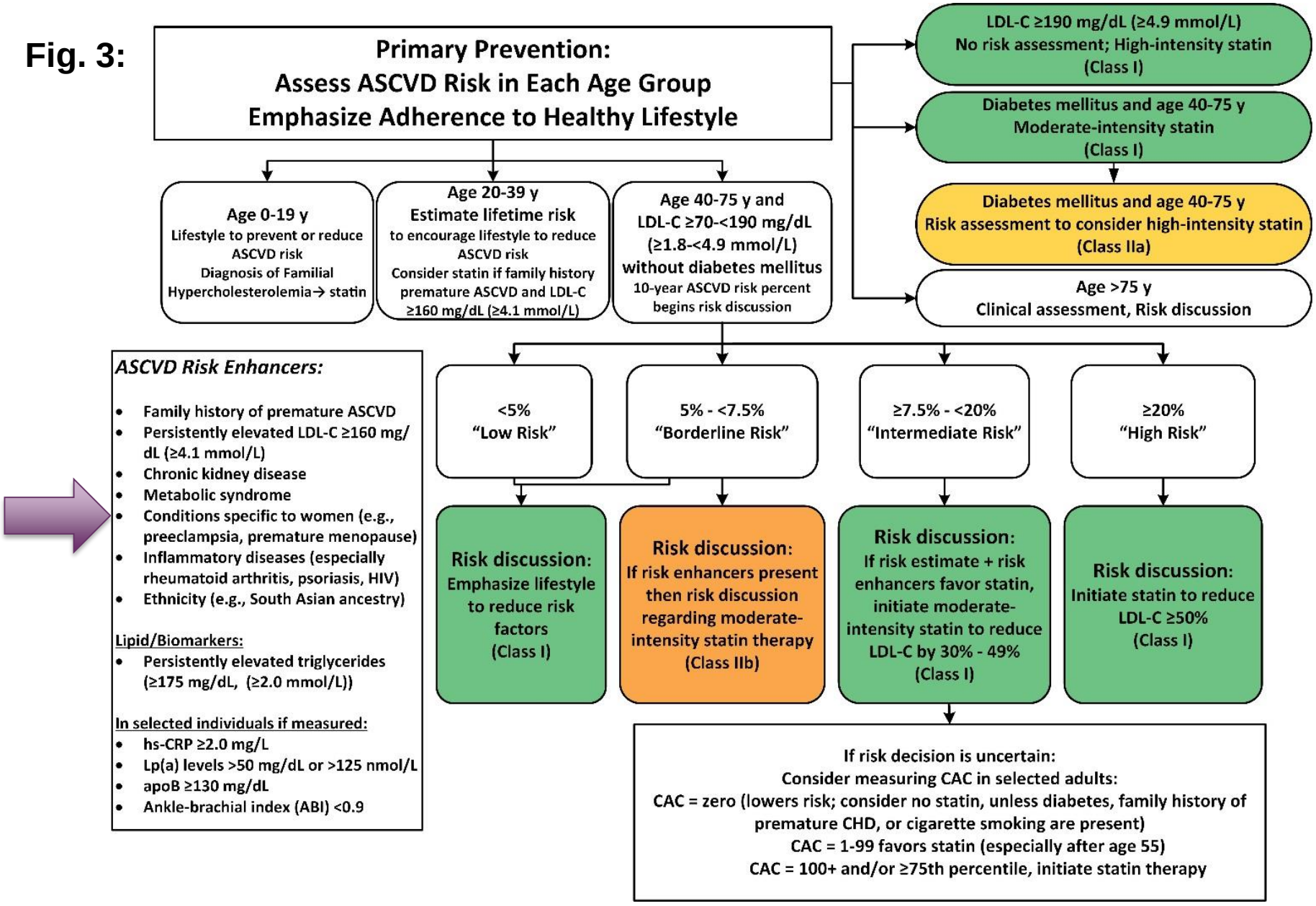


Fig. 3:


Primary Prevention:
Assess ASCVD Risk in Each Age Group
Emphasize Adherence to Healthy Lifestyle
LDL-C ≥190 mg/dL (≥4.9 mmol/L)
No risk assessment; High-intensity statin
(Class I)
Diabetes mellitus and age 40-75 y
Moderate-intensity statin
(Class I)
Diabetes mellitus and age 40-75 y
Risk assessment to consider high-intensity statin
(Class IIa)
Age >75 y
Clinical assessment, Risk discussion
Age 0-19 y
Lifestyle to prevent or reduce ASCVD risk
Diagnosis of Familial Hypercholesterolemia→ statin
Age 20-39 y
Estimate lifetime risk
to encourage lifestyle to reduce ASCVD risk
Consider statin if family history premature ASCVD and LDL-C ≥160 mg/dL (≥4.1 mmol/L)
Age 40-75 y and
LDL-C ≥70-<190 mg/dL (≥1.8-<4.9 mmol/L)
without diabetes mellitus
10-year ASCVD risk percent begins risk discussion
ASCVD Risk Enhancers:
Family history of premature ASCVD
Persistently elevated LDL-C ≥160 mg/dL (≥4.1 mmol/L)
Chronic kidney disease
Metabolic syndrome
Conditions specific to women (e.g., preeclampsia, premature menopause)
Inflammatory diseases (especially rheumatoid arthritis, psoriasis, HIV)
Ethnicity (e.g., South Asian ancestry)
Lipid/Biomarkers:
Persistently elevated triglycerides (≥175 mg/dL, (≥2.0 mmol/L))
In selected individuals if measured:
hs-CRP ≥2.0 mg/L
Lp(a) levels >50 mg/dL or >125 nmol/L
apoB ≥130 mg/dL
Ankle-brachial index (ABI) <0.9
<5%
"Low Risk"
5% - <7.5%
"Borderline Risk"
≥7.5% - <20%
"Intermediate Risk"
≥20%
"High Risk"
Risk discussion:
Emphasize lifestyle to reduce risk factors
(Class I)
Risk discussion:
If risk enhancers present then risk discussion regarding moderate-intensity statin therapy
(Class IIb)
Risk discussion:
If risk estimate + risk enhancers favor statin, initiate moderate-intensity statin to reduce LDL-C by 30% - 49%
(Class I)
Risk discussion:
Initiate statin to reduce LDL-C ≥50%
(Class I)
If risk decision is uncertain:
Consider measuring CAC in selected adults:
CAC = zero (lowers risk; consider no statin, unless diabetes, family history of premature CHD, or cigarette smoking are present)
CAC = 1-99 favors statin (especially after age 55)
CAC = 100+ and/or ≥75th percentile, initiate statin therapy

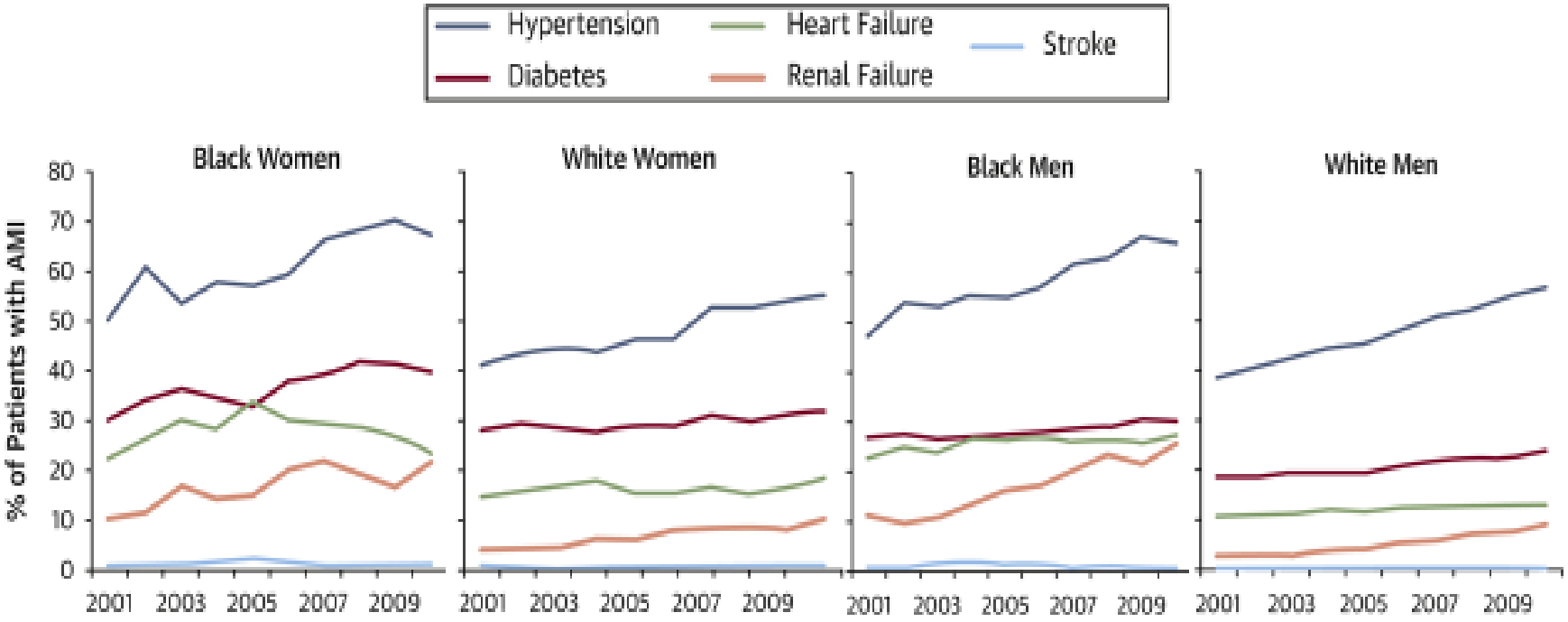
Circulation

February 2019 Go Red For Women® Issue

Twenty Year Trends and Sex Differences in Young Adults Hospitalized with Acute Myocardial Infarction: The ARIC Community Surveillance Study

Sameer Arora MD[1], George A Stouffer MD[1], Anna M. Kucharska-Newton PhD[2], Arman Qamar MD[3], Muthiah Vaduganathan MD MPH[3], Ambarish Pandey MD[4], Deborah Porterfield MD MPH[5], Ron Blankstein MD[3,6]; Wayne D. Rosamond PhD[2], Deepak L. Bhatt MD MPH[3], Melissa C. Caughey PhD[1]

Burden of cardiovascular risk factors has increased among young adults



Gupta et al. J Am Coll Cardiol. 2014;64:337-45

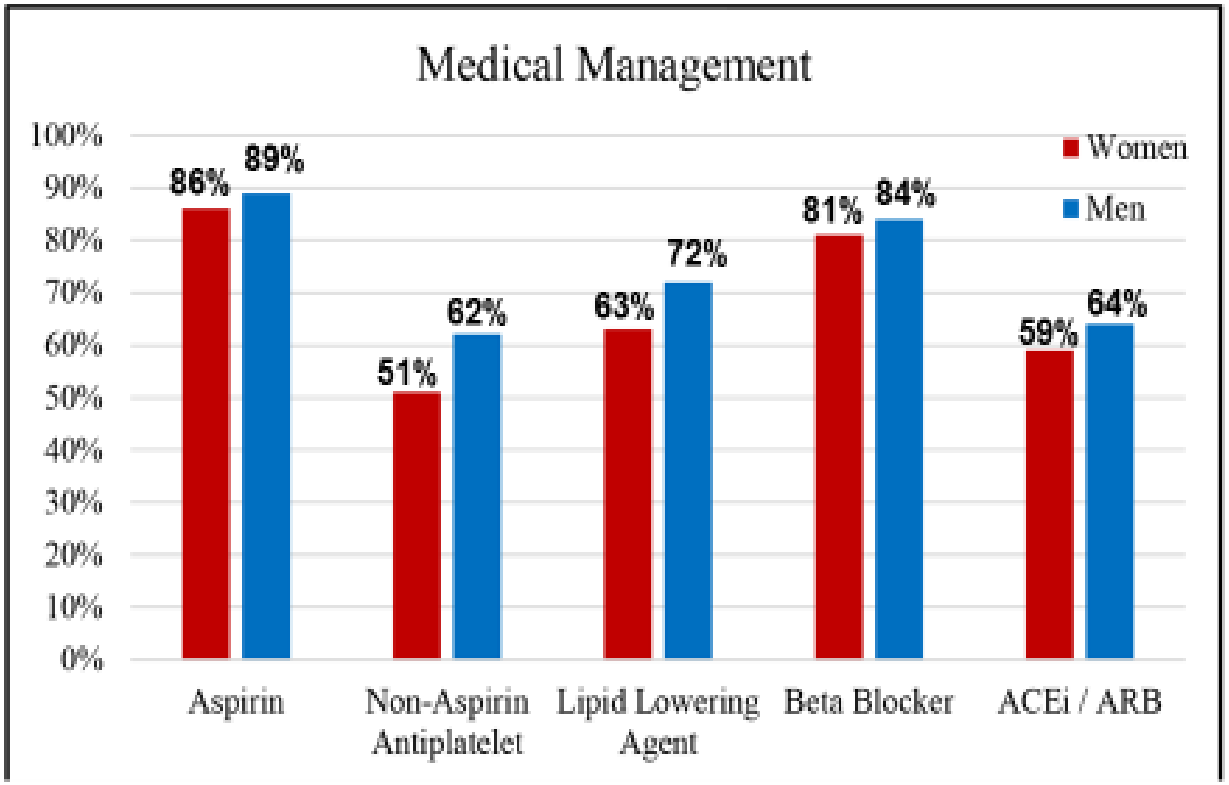
Characteristics of Young Patients with AMI

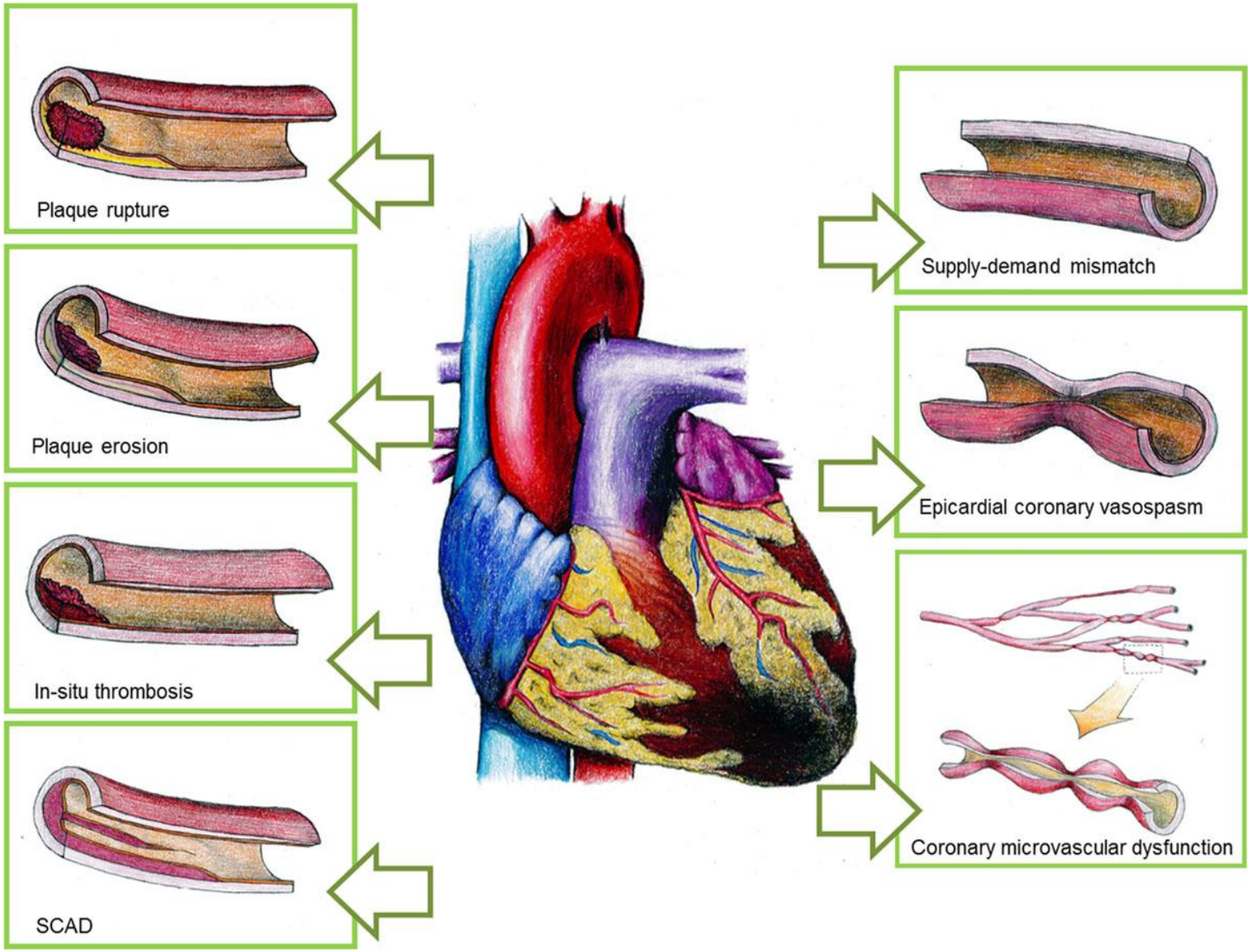
- **Young Women were more likely to be black, to present with non-STEMI and to have higher prevalence of hypertension, diabetes, and prior stroke**

	Women	Men	
Characteristic	N=2884	N=5853	P-value
Age (mean)	48 ± 0.2	48 ± 0.1	0.2
Black	52%	41%	<0.0001
Hypertension	71%	64%	0.0005
Diabetes mellitus	39%	26%	<0.0001
Stroke	10%	6%	0.0003
ST-segment elevation‡	16%	26%	<0.0001

Treatment Disparities: Young Women vs. Men with AMI

- **Young women were less likely to receive evidence-based AMI medications**



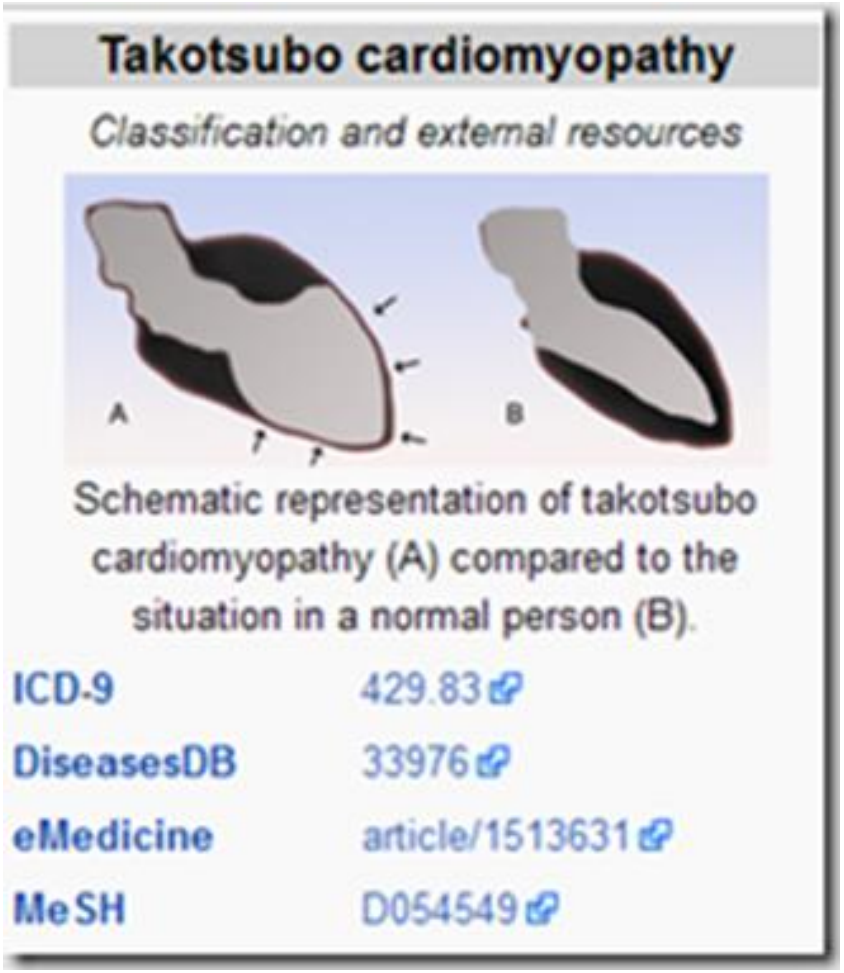

Plaque rupture
Plaque erosion
In-situ thrombosis
SCAD
Supply-demand mismatch
Epicardial coronary vasospasm
Coronary microvascular dysfunction

PLAQUE EROSION VS RUPTURE WOMEN AND ACUTE MI

- In women older than 50 years, plaque rupture is the most common cause of acute MI
  - Associated with hyperlipidemia
  - Plaque is vulnerable with a thin fibrous cap overlying a necrotic core
- In younger women, plaque erosion is more often responsible for infarction
  - Associated with smoking
  - Estrogen may protect against plaque rupture
  - Eroded plaque is rich in smooth muscle cells and proteoglycans
  - Associated with less obstruction and calcification

TAKOTSUBO/ STRESS CM IN WOMEN

- Mainly affects postmenopausal women
- Generally after extreme emotional or exertional trigger
- ACS with no obstructive CAD & effects multiple artery territories



Templin C, NEJM 2015

MICROVASCULAR/ ENDOTHELIAL DYSFUNCTION

- Defined as limited coronary flow reserve and endothelial dysfunction
- Associated with worse outcome
- Increased rate of cardiac death, stroke and heart failure
- Annual MACE event rate of 2.5% in women

Wei J, Mehta PK, Results from WISE, JACC Intervention 2012

MI WITH NONOBSTRUCTED CORONARY ARTERIES (MINOCA)

- MI with nonobstructive CAD
  - found in 6% of all MIs
  - Median age 58
  - 50% women
  - Possibly due to structural dysfunction, vasospasm, and thrombotic disorders
  - Has guarded prognosis with better 12 mo mortality compared to obstructive CD

Beltrame JF, J Intern Med 2013

PREVENTION OF STROKE IN WOMEN

SCOPE OF THE PROBLEM

- 200K more disabled women than men after stroke
- Women are more likely to be living alone & widowed before stroke
- Women are more often institutionalized after stroke & have poorer recovery
- Nearly half of stroke survivors have residual deficits 6 mo after strokes

FIRST STROKE PREVENTION GUIDELINES FOR WOMEN- 2014

Guidelines for the Prevention of Stroke in Women

A Statement for Healthcare Professionals From the American Heart Association/American Stroke Association

The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists.
Endorsed by the American Association of Neurological Surgeons and Congress of Neurological Surgeons

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Table 3. Stroke Risk Factors, Categorized by Those That Are Sex-Specific, Stronger or More Prevalent in Women, or Similar Between Women and Men

Risk Factor	Sex-Specific Risk Factors	Risk Factors That Are Stronger or More Prevalent in Women	Risk Factors With Similar Prevalence in Men and Women but Unknown Difference in Impact
Pregnancy	X		
Preeclampsia	X		
Gestational diabetes	X		
Oral contraceptive use	X		
Postmenopausal hormone use	X		
Changes in hormonal status	X		
Migraine with aura		X	
Atrial fibrillation		X	
Diabetes mellitus		X	
Hypertension		X	
Physical inactivity			X
Age			X
Prior cardiovascular disease			X
Obesity			X
Diet			X
Smoking			X
Metabolic syndrome			X
Depression		X	
Psychosocial stress		X	

KEY POINTS: UPDATE ON 2014 AHA/ASA GUIDELINE FOR PREVENTION OF STROKE IN WOMEN

- Women experience more prevalent stroke, more death from stroke and more disability from stroke
- HTN worse with age & race in women
- Afib associated with higher risk of stroke, cardiac events, and mortality in women

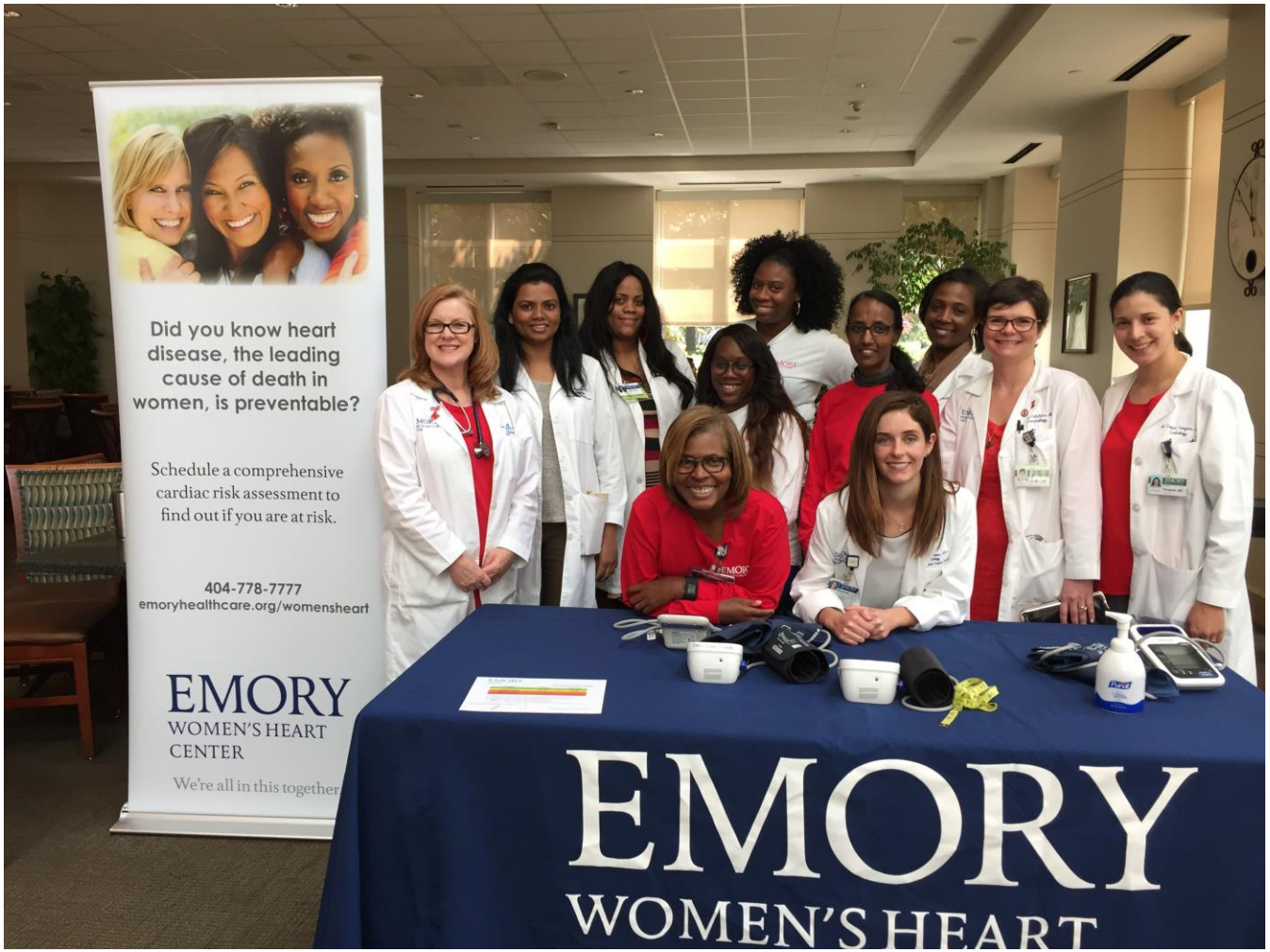
- Women with DM have higher risk of stroke compared to men with DM
- Evidence lacking for stroke risk and abnormal lipids (TC, LDL, HDL, TG)
- Migraine is more common in women & migraine with aura assoc with ischemic stroke
- Estrogen-containing OCP may increase risk of stroke in migraine with aura

SUMMARY- CVD IN WOMEN

Unique risk factors for stroke & heart disease in women:

- Pregnancy- gestational diabetes, preeclampsia, eclampsia,
- Hormone therapy
- More hypertension at ≥age 65 females
- More sedentary, obese females
- More high cholesterol in females

Q&A


Did you know heart disease, the leading cause of death in women, is preventable?
Schedule a comprehensive cardiac risk assessment to find out if you are at risk.
404-778-7777
emoryhealthcare.org/womensheart
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